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AMYRIS OF JAMAICA. NICOTINAMIDES OF AMYRIS PLUMIERI D.C., (RUTACEAE)

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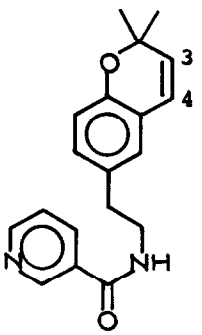
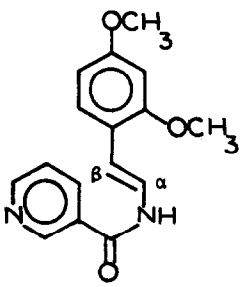
Unlike most rutaceous genera, Amyris[1] has attracted little attention of chemists. Recently however, there have been reports of coumarins in A. simplicifolia[2] and A. madrensis[3], and upon re-examination the essential oil of A. balsamifera[4] has yielded several sesquiterpenes. We now describe the formulation of two nicotinamides found among products from the benzene extract of the Jamaican variety[5] of Amyris plumieri a plant which on botanical grounds was placed in the family Burseraceae[6] but which has been reclassified as Rutaceae[1].

The chromene I, $C_{19}H_{20}N_2O_2$, m.p. 99-100°, was characterised on the basis of its spectral data. UV maxima at 224.5, 263.5 and 315 (log ε 4.43, 3,84, 3.32 respectively) nm indicated a chromene and other aromatic moiety, while IR bands at 3225 and 1653 cm^{-1} suggested amide.



I.

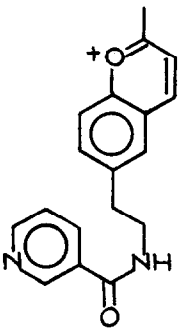
II. 3,4,-dihydro



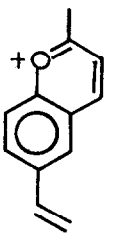
III.

IV. α,β-dihydro

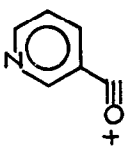
The ^{1}H NMR (60 MHz) spectrum of I in $CDCl_3$ gave signals at δ 1.43 (6H, singlet) and 5.58 and 6.25 (each 1H, doublet, J = 9 Hz) for the hetero portion of the 2,2-dimethyl chromene. Signals at δ 2.81 (2H, triplet, J = 7 Hz), 3.67 (2H, quartet, J = 7 Hz, collapsing to triplet, 2 H, after shaking with D_2O) and 6.80 (1H, vanishing after exchange with D_2O) indicated the moiety $ArCH_2CH_2NHCO$-, while four low field protons, located at δ 7.52 - 8.83 were characteristic of a nicotinamide group[7]. The substitution pattern on the aryl portion of the chromene was revealed by signals at δ 6.65 (1H, doublet, J = 8 Hz), 6.78 (1H, doublet, J = 2 Hz) and 6.91 (1H, doublet of doublets, J = 8, 2 Hz).



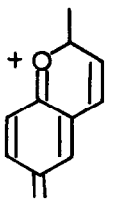
(a) m/e 293



(b) m/e 171



(c) m/e 106



(d) m/e 158

Figure I

Together with others, the fragments a - d (Figure I) obtained from mass spectral analysis of I supported these gross features.

Hydrogenation of I over 10% Pd/C gave the dihydroderivative II, $C_{19}H_{22}N_2O_2$, m.p. 125-128°; λ_{max} 226 and 264 (log ε 4.20 and 3.82 respectively) nm. The IR and ^{1}H NMR (60 MHz) spectra supported the structure II.

The structure I was finally confirmed to be a 6-substituted chromene by a biogenetic type synthesis via prenylation of the nicotinamide derivative of tyramine.

Compound III, $C_{16}H_{16}N_2O_3$, m.p. 159-160° had UV maxima at 265.5 and 366.6 (log ε 3.31 and 3.50 respectively) nm. IR bands at 3177, 1653 and 1605 cm^{-1} indicated amide and aryl moieties. Immediately obvious from the ^{1}H NMR (60 MHz) spectrum of III in $CDCl_3$ were the signals for the nicotinamide segment. In addition, there were signals at δ 6.47 (1H, doublet, J = 14.5 Hz) and 7.63 (1H,

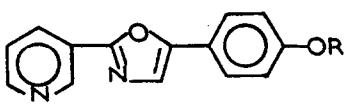
doublet of doublets, J = 14.5, 10 Hz, collapsing to a doublet J = 14.5 Hz upon shaking the sample with D_2O) for the vinyl protons of the group ArCH = CH-NH-CO-. One benzenoid proton partially overlapped with those of the heteroaromatic ring while the other two appeared as a multiplet at δ6.54.

Further confirmation of the styrylamide grouping was obtained upon hydrogenation of III with 10% Pd/C in ethanol to give IV, $C_{16}H_{18}N_2O_3$, m.p. 112-113°. The UV [215.5, 271 (log ε 4.14 and 3.73 respectively) nm] and the IR (3344 and 1661 cm^{-1}) spectra of IV were consistent with the change, while the ^1H NMR spectrum showed the signals for $ArCH_2CH_2NH$ CO- at δ2.90 (2H, triplet, J = 6 Hz), 3.72 (2H, quartet, J = 6 Hz, collapsing to a triplet, 2H, after shaking the sample with D_2O) and an exchangeable proton at δ6.48 (1H, broad multiplet).

Ozonolysis of III to yield 2,4-dimethoxybenzaldehyde and synthesis of IV from the latter compound confirmed the gross structure of III. The trans-geometry of the styryl linkage was based on the coupling constant (J = 14.5 Hz) of the olefinic protons.

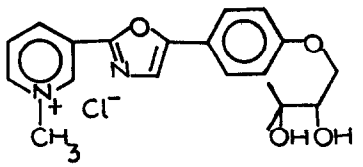
The presence of the chromene and amide[8] moieties in Amyris plumieri supports the botanical classification of the species as rutaceous.

This was confirmed by the discovery in the same plant of the masked nicotinamide O-dimethylallyl halfordinol, V, an oxazole, derivatives of which have been



V. R = $CH_2CH = C(CH_3)_2$

VI. R = $CH_2CH_2C(CH_3) = CH_2$



VII.

found only in the Rutaceae. Compound V had m.p. 115-118°; the UV absorption [λ_{max} 250, 261 and 327.5 (log ε4.06, 4.03 and 4.40 respectively) nm] gave a bathochromic shift in acid to 261 and 346 (log ε 4.21 and 4.24 respectively) nm, and IR bands were at 1616, 1605, 1582 and 822 cm^{-1}. The ^1H NMR spectrum showed the presence of a 3-substituted pyridine (4 protons between δ 7.43 and 9.47) a p-disubstituted benzenoid ring (δ 6.44, 8.44, 2H each, doublets, J = 9 Hz) and a 3,3-dimethylallyl ether (δ 1.80, 6H, broad singlet, 4.70, 2H doublet, J = 6.5 Hz coupled to a triplet, 1H, at δ 5.62). The oxazole proton was a sharp singlet at δ 7.47. These properties coincide with those reported by Dreyer[9] for V, which was found in a mixture with O-isopentenyl isomer VI, and can be related to those of N-methyl halfordinium chloride VII[10].

The compounds I and III are the first reported unmasked nicotinamides in Rutaceae.

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